REMARKS

In view of the following remarks, the Examiner is requested to allow Claims 1-68, the only claims pending and under examination in this application.

Claim Rejections – 35 U.S.C § 112, first paragraph

The Examiner has rejected Claims 1-68 under 35 U.S.C. § 112, first paragraph as allegedly lacking written description and/or enablement. This rejection is respectfully traversed.

As a preliminary matter, the Applicants would like to point out that although the Office characterizes the present rejection as a written description rejection, the Office's use of the *In re Wands* factors in support the rejection indicates to the Applicants that the rejection is in fact an enablement rejection and not a written description rejection. Hence, as the basis of the rejection is unclear, and the Applicants cannot determine if the present rejection constitutes a new rejection or not, the Applicants respectfully request that the finality of this rejection be withdrawn. According to the M.P.E.P. § 706.07 (a), a final rejection is not proper where a new ground of rejection is introduced in a subsequent Office Action unless the new ground of rejection was necessitated by amendment. Consequently, the Applicants seek clarification and respectfully request that the finality of this rejection be removed.

According to the M.P.E.P §§ 2164.01 and 2164.08, the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent application coupled with information known in the art without undue experimentation. The Federal Circuit has repeatedly held that the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'. Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. Hence, all that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See also, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

With respect to the present rejection, the Office appears to be asserting that the rejected claims are not enabled on the grounds that: 1) the state of the art is unpredictable; 2) undue experimentation would be required to practice the claimed invention; and 3) the claims are overly broad. For the reasons stated herein below the Applicants respectfully disagree.

The State of the Art is Not Unpredictable

It is to be noted that the Office has once again mischaracterized the nature of the instant invention. Specifically, although the Office asserts that the present invention is directed to a method of augmenting human skin fibroblast, the Office also indicates that any of a wide representation of soft and hard tissue is capable of being *treated* by the above method.

The Applicants, however, would like to point out that the rejected claims are not directed to *treating* soft or hard tissue, or for that matter, to skin fibroblast per se. On the contrary, the rejected claims are simply directed to *augmenting*, for instance, adding to, soft or hard tissue by contacting the soft or hard tissue with the claimed biological adhesive materials, i.e., the cross-linkable components recited in the claims. According to the specification, the strength of the combined biological adhesive materials was tested and found to be useful in affecting tissue augmentation in general. See paragraphs 178-180, 222 and 223. Hence, whether it is soft or hard tissue that is being augmented is not determinative of the capability of the recited biological adhesives add to or otherwise augment the tissue.

That is, the type of tissue does not determine the functionality of the biological adhesive materials. Rather, it is the interaction between the nucleophilic and electrophilic groups of the cross-linkable components of the adhesives that are determinative of augmentation. For instance, once inside a patient's body the nucleophilic groups on the first polymer and the electrophilic groups on the second polymer react with one another to cross-link and thereby form a polymer network *in situ*. See paragraph 180. This happens regardless of whether the tissue is soft or hard tissue. Therefore, contrary to the assertion of the Office, the subject invention is not directed to *treating* soft and hard tissue; rather, the subject invention is directed to a method for using the recited cross-linkable components to *augment* or add to soft or hard tissue.

The Applicants contend that as set forth in the Background of the Invention, the state of the art with respect to adhesives, biological adhesive materials in particular, is well developed and predictable. For instance, the Applicants would like to draw the attention of the Office to the extensive research that has been performed in the biological adhesive arts, as evidenced by the numerous references cited in the Background section of the specification. Specifically, U.S. Patent Nos. 5,162,430; 5,324,775; 5,328,955; 5,580,923; and 5,614,587 set forth biomaterial compositions, such as collagen-synthetic polymer conjugates, that are capable of cross-linking to effect adhesion.

Additionally, the Applicants would like to draw the attention of the Office to the high degree of development pertaining to the use of cross-linkers in biological applications that is set forth throughout the Applicants' entire specification. Specifically, the specification discloses a detailed discussion of the chemical reactions that the two recited components of the invention undergo (pp. 6-7). Further, the specification discloses a long list of the first and second cross-linkable components that may be used in accordance with the claimed invention. For instance, the specification sets forth exemplary synthetic components with multiple nucleophilic groups (pp. 8-10); exemplary synthetic components with electrophilic groups (p.10); exemplary hydrophilic components (pp. 10-12); and exemplary hydrophilic components (pp. 12-13) that may all be used in accordance with the methods of the invention. The specification further sets forth a discussion of the preparation of crosslinked polymer compositions (pp. 13-15); a discussion of administration of the crosslinked synthetic polymer compositions (pp. 18-19); a discussion of the use of the crosslinked synthetic polymer compositions in tissue augmentation (pp. 24-25); seven examples (pp. 27-34); and 18 figures with related discussions pertaining to each.

Accordingly, the Applicants contend that in view of what was known in the art at the time of filing and in view of the teachings of the specification, one of skill in the biological adhesive arts would be able to use the claimed biological adhesive materials in the claimed methods in a routine and predictable manner so as to attain the objects of the present invention, regardless of the soft or hard biological tissues to which the adhesives are applied. The Office has not set

forth any reason as to why one of ordinary skill in the art would expect that the type of tissue, e.g., a particular hard or a particular soft tissue, would in any way affect the ability of the claimed biological adhesives to cross-link and thereby function in augmenting that tissue. Therefore, contrary to the assertion of the Office, the state of the biological adhesive arts is not unpredictable.

Undue Experimentation is Not Required to Practice the Claimed Invention

Additionally, the Office asserts that one of ordinary skill in the art would have to engage in undue experimentation in order to practice the claimed invention. Specifically, the Office asserts that in order to practice the claimed invention one would first need to determine the type of soft and hard tissue to be *treated.* The claimed invention, however, is directed to a method of *augmenting* soft or hard tissue and not to *treating* soft or hard tissue. As set forth above, the type of soft or hard tissue is not determinative of the functionality of the biological adhesive materials used in augmenting that tissue. The only experimentation that would be required to determine if a tissue is "hard" or "soft" would be to feel that tissue. Given the extensive training that medical doctors go through to attain their license to practice, the Applicants contend that this is well within the skill set of the ordinary practitioner. Specifically, the Applicants contend that one of ordinary skill in the art could readily determine if a given tissue was soft or hard without undue experimentation.

The Claims Are Not Overly Broad

Further, the Office asserts in Section (7) that the claims are *extremely* broad given the vast number of possible soft and hard tissues encompassed by the instant invention. The Applicants, however, respectfully disagree. As described above, the type of soft or hard tissue does not determine the ability of the first and second cross-linkable components to cross-link *in situ.* Rather, it is the presence of $n \geq 2$ electrophilic groups on one component and $m \geq 2$ nucleophilic groups on the other component that allows them to engage in a cross-linking reaction. The Applicants have characterized this reaction and set forth the reaction dynamics at paragraphs 33-71. Additionally, the Applicants have set forth several exemplary electrophilic and nucleophilic

polymers that cross-link when combined and may be used in accordance with the claimed invention. See for instance paragraphs 85-115 and 78-83. Furthermore, the Applicants have set forth several examples wherein exemplary electrophilic and nucleophilic polymers were combined and shown to crosslink. See paragraphs 196-219 and 222-234. Accordingly, the Applicants contend that the claims are not overly broad given the extensive teachings, the exemplary polymers to be used, and the actual experimental results set forth in the disclosure of the specification.

The Office, however, in its response to the Applicants' remarks filed on January 29, 2007, asserts that the Applicants expect the artisan to go on a fishing voyage to identify any and all the compounds that would work in the Applicants' claimed invention. The Office appears to be asserting that the claims are overly broad on the ground that because the Applicants have not set forth each and every compound that meets the limitations of the claims.

The Applicants, however, respectfully disagree and contend that the Office is applying an improper standard in support of this rejection. As set forth in M.P.E.P § 2164.08, not everything necessary to practice the invention need be disclosed in the specification. See also: *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). Rather, the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. Hence, all that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art.

Accordingly, the Applicants contend that the requirement of the Office that the Applicants "identify any and all the compounds, known or yet to be discovered" that meet the limitations of the claims is erroneous. Further, the Applicants contend that given the extensive teachings, the exemplary polymers to be used, and the actual experimental results set forth in the disclosure of the specification, as well as what was well known to those of skill in the art at the time of the Applicants' filing, the scope of the claims does in fact bear a "reasonable correlation" to the scope of enablement.

Therefore, in view of the above, the Applicants contend that the state of the relative art is well-developed and predictable, undue experimentation is not required in practicing the claimed invention, and the claims are not overly broad. Consequently, the Applicants contend that the rejected claims are enabled within the meaning of 35 U.S.C. § 112, first paragraph, and respectfully request that this rejection be withdrawn.

Claim Rejections – 35 U.S.C § 112, first paragraph

The Examiner has rejected various unspecified claims under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. This rejection is respectfully traversed.

As a preliminary matter, the Applicants would like to point out that it is unclear as to whether this rejection is a separate and distinct rejection from the enablement rejection recited above. For instance, the Office appears to characterizes this rejection as a written description rejection. However, this rejection was not advanced in the previous Office Action, and, therefore, appears to be a new ground for rejection. According to the M.P.E.P. § 706.07 (a), a final rejection is not proper where a new ground of rejection is introduced in a subsequent Office Action. Consequently, the Applicants seek clarification and respectfully request that the finality of this rejection be removed.

Additionally, the Applicants would like to draw the attention of the Office to Claim 1 of U.S. Patent No. 6,534,591. The '591 patent is a parent of the present application. Claim 1 reads as follows:

> 1. A crosslinkable composition comprised of:
> (a) a first crosslinkable component having m nucleophilic groups, wherein m≧2;
> (b) a second crosslinkable component having n electrophilic groups capable of reaction with the m nucleophilic groups to form covalent bonds, wherein n≧2 and m+n≧5,

As can be seen with reference to the above, the language deemed by the Office to be objectionable with respect to the present application, has already been found acceptable for 35

U.S.C. § 112 purposes, with respect to the parent application, which has now issued as U.S. Patent No. 6,534,591. Accordingly, for the purposes of promoting consistent prosecution the Applicants respectfully request that the present rejection be withdrawn as the language objected to has already been found to be acceptable by the Office, as evidenced by the issuance of the '591 patent.

The above not withstanding, the Office asserts that there is no written description in the specification for each of m and n > 5. The Applicants, however, respectfully disagree and would like to draw the attention of the Office to paragraphs 15 and 34-35, which is set forth herein below:

> **[0015]** In a general method for preparing a composition for the delivery of a negatively charged compound (such as a protein or drug), a first synthetic polymer containing two or more nucleophilic groups is reacted with a second synthetic polymer containing two or more electrophilic groups, wherein the first synthetic polymer is present in molar excess in comparison to the second synthetic polymer, to form a positively charged matrix, which is then reacted with a negatively charged compound. In a general method for preparing a matrix for the delivery of a positively charged compound, a first synthetic polymer containing two or more nucleophilic groups is reacted with a second synthetic polymer containing two or more electrophilic groups, wherein the second synthetic polymer is present in molar excess in comparison to the first synthetic polymer, to form a negatively charged matrix, which is then reacted with a positively charged compound.

[0034] polymer - X_m + polymer - Y_n ⟶ polymer - Z – polymer

[0035] wherein m > 2, n > 2, and m + n > 5;

As can be seen with reference to the above paragraphs, the specification clearly sets forth support for the recitation within in the claims that the nucleophilic group (m) is two or more, the electrophilic group (n) is two or more, and m + n > 5. Accordingly, the Applicants contend that contrary to the assertion of the Office there is in fact support for each of m and n > 5. Consequently, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

The Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

By: _____

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